REMARKS

CLAIM STATUS

Claims 29-33 are pending in the application.

Rejection Under 35 U.S.C. §103

Claims 29-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Columbo et al. (J. Immunol. 160:2780-2785 (1998)) in view of Pauli et al. (Clinical and Experimental Allergy, 30:1076-1084 (2000)).

The Examiner contends that since Columbo et al. teach the 1-30 IgE epitope of Par j 1 and Par j 2 is a conformational, discontinuous epitope, it would have been obvious to perform mutational analysis at the positions taught by Columbo et al. to generate a Par j 1/ Par j 2 multimer protein with reduced IgE binding at that epitope. The rejection is respectfully traversed.

Applicants submit that Colombo et al. only teach the cysteines in positions 14 and 29 are essential for IgE binding (*see* paragraph "epitope mapping" from p. 2781 to p. 2782), and that single mutation of K21, K23, E24 or K27 causes loss of binding (*see* p. 2782, left column, second paragraph, Fig. 3A and 3B). The Examiner may argue that it would be obvious to perform mutational analysis on the various combinations of mutations suggested by Colombo. Obvious to try, however, is not the test for obviousness.

Furthermore, Colombo et al. have not provided a reasonable expectation of success on the effect of multiple mutations on the Parj 1 molecule. Colombo et al. do not present any data on the effect of more than one mutation on the Parj 1-derived 30 amino acids peptide. If the Examiner contends that it is reasonable to expect success with multiple mutations on the mutated Parj 1 molecule, it is also equally plausible to expect failure with multiple mutations on the Parj 1 molecule. As acknowledged by the Examiner, the 1-30 IgE epitope of Par j 1 is a conformational epitope. Applicants submit that the effects of multiple mutations on a conformational epitope need to be determined empirically. Applicants would like to direct the Examiner's attention to two papers describing the site-specific mutagenesis of the amino acid residues on the Parj 1 allergen.

The paper by Bonura et al. (Int. Arch. Allergy Immunol. 126:32-40 (2001)) teaches that cysteine substitution did not necessarily lead to allergens with reduced allergenicity. The paper also teaches that substitution of cysteines 50 and 52 did not cause a reduced IgE binding activity *in vitro* and *in vivo*. On the other hand, mutagenesis on cysteines 4, 29 and 30 dramatically affected the IgE binding activity.

In addition, the paper by Colombo et al. (J. Immunol. 160:2780-2785 (1998)) teaches that the single Q19 and E22 substitutions did not reduce IgE binding activity in the region of amino acid residues 1-30. The single K21, K23, E24 and K27 substitution did.

These results could not have been predicted by one of ordinary skill in the art at the time of the invention without performing the necessary experiments.

Further support for lack of reasonable expectation of success comes from the teaching of Pauli et al. The homodimer Betv1-Betv1 and homotrimer Betv1-Betv1-Betv1 are shown to induce no reaction at a concentration of 10 ug/ml in the prick test (*see* Pauli at p. 1079, left column, first paragraph and Fig. 2). In addition, the Betv1 homotrimer seems to be hypoallergenic after intradermal testing of birch allergic patients (*see* Fig. 3b and Fig. 4a). Pauli indicates, however, at p. 1081, right column, last sentence to p. 1082, left column, first sentence that: "*one has to consider that the absence of local reactions during intradermal testing cannot predict the absence of systemic effects during immunotherapy*".

Applicants submit that the present invention of making a molecule possessing hypoallergenic properties by merging two independent allergens (Parj1 + Parj2), each of which has multiple mutations in the IgE epitope, is not obvious in view of the references cited by the Examiner.

In view of the above remarks, Applicants respectfully request that the rejection of claims 29-33 under 35 U.S.C. 103(a) be withdrawn.

If a telephone interview would be of assistance in advancing prosecution of the subject application, Applicants' undersigned attorney invites the Examiner to telephone him at the number provided below. No fee is deemed necessary in connection with the filing of this Communication. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 50-1891.

Respectfully submitted,

Albert Wai Kit Chan

Albert Wai-Kit Chan
Registration No. 36,479
Attorney for Applicants
Law Offices of
Albert Wai-Kit Chan, PLLC
World Plaza, Suite 604
141-07 20th Avenue
Whitestone, New York 11357
Tel: (718) 799-1000
Fax: (718) 357-8615
E-mail: chank@kitchanlaw.com